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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/565,533	12/13/2006	Robert Andrew Slade	GJE-0001 (049038-013)	2151

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EXAMINER	
BURK, CATHERINE E	
ART UNIT	PAPER NUMBER
3735	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/565,533	SLADE ET AL.	
	Examiner	Art Unit	
	CATHERINE E. BURK	3735	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *23 November 2010*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-55,66 and 67* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-55,66 and 67* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *18 January 2006* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *See Continuation Sheet*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

Continuation of Attachment(s) 3). Information Disclosure Statement(s) (PTO/SB/08), Paper No(s)/Mail Date :25 April 2006, 29 March 2010, 9 November 2010.

DETAILED ACTION

1. This action is responsive to the amendment filed on November 23rd, 2010. The examiner acknowledges the amendments to claims 1 and 13 and the cancellation of claims 56-65. Claims 1-55, 66, and 67 are pending. Also, the examiner has withdrawn the previous restriction requirement because the claims as currently amended form a single general inventive concept, accordingly, claims 1-55, 66, and 67 have been examined on the merits.

Claim Rejections - 35 USC § 101

2. 35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

3. Claims 37-55 are rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter.

4. Claim 37 recites the limitation "one or more magnetic particles localized at or in the material in the working volume". In this invention, the working volume may be a cancerous site in a patient; therefore the particles are claimed as being localized within a patient. A claim directed to or including within its scope a human is not considered to be patentable subject matter under 35 U.S.C. 101. The grant of a limited, but exclusive property right in a human being is prohibited by the Constitution. In re Wakefield, 422 F.2d 897, 164 USPQ 636 (CCPA 1970). The claim should be amended to state the magnetic particles are adapted to be localized at or in the material in the working volume.

Claim Rejections - 35 USC § 102

5. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

6. Claims 1-5, 7-11, 13-17, 19, 20, 22-26, 28, 29, 31-33, 37-44, 46-48, 50-54, 66, and 67 are rejected under 35 U.S.C. 102(b) as being anticipated by Kraus (US 6470220 B1).

7. Claims 1 and 13; Kraus discloses a method for disrupting a tissue structure comprising administering one or more magnetic particles to a subject and localizing the particles to the tissue (col. 3, line 63-col. 4, line 5). Treatment is carried out by applying a magnetic field to the tissue where the particles are located, the field causing the particles to rotate and thereby disrupt the structure of the tissue (col. 11, lines 53-59 and col. 13, lines 9-62). The particles may be made from rare-earth magnet material which exhibits a large magnetization such as samarium-cobalt (Sm-Co) or neodymium-iron-boron (Nd-Fe-B) (col. 12, lines 15-20 and col. 4, lines 19-25). According to applicant's specification at the bottom of p. 12 and the top of p. 13, rare-earth alloys such as samarium-cobalt have inherently high magneto-crystalline anisotropy; therefore particles made of this material are stabilized by magnet crystalline anisotropy. Kraus discloses the magnetic field is applied by a magnetic field generator comprising a plurality of coils and a control system for causing a change in the magnetic field for inducing particle rotation (fig. 1 and col. 13, lines 16-25).

8. Claims 2 and 14-16; the tissue is biological material and may be a mammalian cell (col. 1, lines 9-13).

9. Claims 3 and 17; the tissue may be a tumor (col. 3, lines 4-6).

10. Claims 4, 5, 19, and 20; the particles may comprise a targeting moiety such as an antibody (col. 4, lines 30-34).

11. Claims 7 and 22; magneto-crystalline anisotropy is a physical property of a material. According to applicant's specification at Table 1, samarium-cobalt has a magneto-crystalline anisotropy of 10,000 kJ/m^3 or 1 x 10^7 J/m^3.

12. Claims 8 and 23; samarium-cobalt is a rare-earth metal alloy (col. 4, lines 19-24).

13. Claims 9 and 24; the particle may comprise a coating of a biocompatible material (col. 12, line 65 - col. 13, line 4).

14. Claims 10, 11, 25, and 26; an exemplary particle diameter is 100nm (col. 8, lines 47-50 and col. 10, lines 49-52).

15. Claim 28; the applied magnetic field has a flux density from 0.01-0.1 Tesla (col. 11, lines 40-41).

16. Claim 29; the magnetic field is varied in a sinusoidal fashion and has a smoothly varying current profile (col. 13, lines 20-26), therefore the variation is continuous.

17. Claim 31; after a period of continuous field variation, the field is turned off for a predetermined wait period to allow for relaxation and randomization of the magnetic axes of the particles (col. 7, lines 41-46). This process is repeated throughout treatment (col. 7, lines 53-56).

18. Claim 32; the field variation is achieved by suitably controlling an external magnetic field generator (col. 13, lines 20-25).

19. Claim 33; the field can be varied at a frequency of 100 Hz (col. 14, lines 17-21).

20. Claims 66 and 67; according to table 3 of applicant's specification, the flux density required to generate 100pN force couple in 100nm samarium-cobalt spheres is 0.036 Tesla. Kraus discloses 100nm samarium-cobalt spheres (col. 4, lines 19-24 and col. 8, lines 47-50) and

supplying a flux density of up to 0.1 Tesla, therefore, in Kraus' method, the particles will be rotated to exert a force of at least 100pN.

21. Claim 37; Kraus discloses an apparatus for disrupting tissue comprising a magnetic field generator for generating a magnetic field in a working volume containing the tissue and a plurality of magnetic particles localized within the tissue. The magnetic particles may be made from rare-earth magnet material which exhibits a large magnetization such as samarium-cobalt (Sm-Co) or neodymium-iron-boron (Nd-Fe-B) (col. 12, lines 15-20 and col. 4, lines 19-25). According to applicant's specification at the bottom of p. 12 and the top of p. 13, rare-earth alloys such as samarium-cobalt have inherently high magneto-crystalline anisotropy; therefore particles made of this material are stabilized by magnet crystalline anisotropy. Kraus further describes a control system for causing a change in the magnetic field in the working volume with respect to the cancerous tissue so as to rotate the magnetic particles (col. 13, lines 16-25).

22. Claims 38-40; the control system causes rotation of the magnetic field (col. 13, lines 18-25); this constitutes movement (claim 38), or relative rotation (claim 39), between the magnetic field direction and the tissue being treated. This also demonstrates that the control system is adapted to cause the magnetic field vector in the working volume to change in direction (claim 40).

23. Claim 41; the control system may also physically move coils or magnets of the magnetic field generator in order to create the rotating magnetic field (col. 13, lines 10-14). This constitutes causing the magnetic field generator to change relative to the material.

24. Claim 42; the controller pulses the amplitude of the magnetic field in the working volume at various frequencies (col. 7-9 and 17-21).

25. Claim 43; the working volume is located externally to the magnetic field coils (fig. 1).

26. Claim 44; the magnetic field generator comprises a plurality of electromagnets (fig. 1 and col. 13, lines 18-20).

27. Claim 46; the magnetic field generated by the magnetic field generator has a flux density from 0.01-0.1 Tesla (col. 11, lines 40-41).

28. Claims 47 and 48; the particles may comprise a targeting moiety such as an antibody (col. 4, lines 30-34).

29. Claim 50; magneto-crystalline anisotropy is a physical property of a material. According to applicant's specification at Table 1, samarium-cobalt has a magneto-crystalline anisotropy of 10,000 kJ/m^3 or 1×10^7 J/m^3.

30. Claim 51; samarium-cobalt is a rare-earth metal alloy (col. 4, lines 19-24).

31. Claim 52; the particle may comprise a coating of a biocompatible material (col. 12, line 65 - col. 13, line 4).

32. Claims 53 and 54; an exemplary particle diameter is 100nm (col. 8, lines 47-50 and col. 10, lines 49-52).

Claim Rejections - 35 USC § 103

33. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

34. Claims 6, 21, and 49 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kraus in view of Sapra (Cancer Research 62, 7190-7194, 2002).

35. Claims 6, 21, 49; Kraus is silent as to whether the antibody is a cell-internalizing antibody, however Sapra discloses that when liposomal drugs linked to antibodies are targeted to internalizing epitopes on a cell surface, a higher concentration of drug will be delivered to the cell (p. 7190, right column top paragraph). Accordingly, if the magnetic particles of Kraus' invention are linked to cell-internalizing antibodies, a higher concentration of magnetic particles will wind up inside the cell; this would lead to better targeting of treatment. It would have been obvious to one of ordinary skill in the art at the time of the invention to use cell-internalizing antibodies in Kraus' invention because the treatment provided would be more effective due to the higher concentration of magnetic particles inside the cells of the cancerous tissue.

36. Claims 12, 18, 27, and 55 is rejected under 35 U.S.C. 103(a) as being unpatentable over Kraus in view of Fredriksson (WO 01/017611 A1).

37. Claims 12, 27, and 55; Kraus fails to disclose the particles have a cuboid, oblate spheroid, or prolate spheroid shape. However, Fredriksson discloses a method of disrupting tissue using magnetic particles caused to rotate/ vibrate using an externally applied magnetic (p. 3, line 35 - p. 4, line 7). The magnetic particles have an oblate or prolate spheroid shape (figs. 1A-C). It would have been obvious to one of ordinary skill in the art at the time of the invention to use magnetic particles having oblate or prolate spheroid shape because Fredriksson teaches that these shapes are appropriate for disrupting biological tissue under the influence of an external magnetic field.

38. Claim 18; Kraus is silent as to whether the method is carried out in vitro. However, Fredriksson discloses the method described above may be carried out in vivo or in vitro (p. 3, lines 19-21). It would have been obvious to one of ordinary skill in the art at the time of the invention to carry the method out in vitro if this method is being performed as an experiment in a laboratory setting.

39. Claims 30, 34, and 36 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kraus in view of Handy (US 2003/0032995 A1).

40. Claims 30 and 34; Kraus is silent as to the magnetic field being repeatedly applied after re-orienting the material. However, Handy discloses a method of disrupting tissue using magnetic particles under the control of external magnetic fields [0016] similar to Kraus. In Handy's method, a patient is placed upon an X-Y horizontal and vertical axis positioning bed controlled by a controller -108- and the position of the bed and parameters of the magnetic treatment field can be adjusted via a control panel -120- while the location and concentration of magnetic particles can be monitored using magnetic resonance imaging (MRI) or a superconducting quantum interference device (SQUID) [0044]. Since Handy's device has these capabilities, it would have been obvious to one of ordinary skill in the art at the time of the invention to stop treatment and reapply the magnetic treatment field after reorienting or moving the patient based on data obtained by the imaging modality or SQUID and/or if treatment is required at more than one location.

41. Claim 36; Kraus discloses detecting the magnetic particles using SQUID sensors but does not explicitly disclose obtaining a magnetic resonance image of the particles prior to causing

movement of the particles. However, Handy also contemplates the step of imaging at least one of the particles prior to administering treatment with the external magnetic field using, for example, magnetic resonance imaging [0044]. It would have been obvious to one of ordinary skill in the art at the time of the invention to include the step of obtaining an MRI of the particles prior to treatment in the method disclosed by Kraus because Handy discloses the image can be used to define parameters of the treatment such as location, duration, and/or intensity [0044].

42. Claim 35 is rejected under 35 U.S.C. 103(a) as being unpatentable over Kraus in view of Handy as applied to claims 30 and 34 above, and further in view of Dobbs (US 6148058 A).

43. Kraus in view of Handy do not disclose rotating the patient, or the material being treated within the patient. However, Dobbs discloses a rotating computed tomography (CT) system comprising a rotatable platform for supporting a patient and rotating the patient through an x-ray scanning field in order to image a full rotation of the patient (col. 3, lines 52-60, col. 5, lines 36-44, and col. 6, lines 2-3). It would have been obvious to one of ordinary skill in the art at the time of the invention to modify the imaging modality used in Kraus in view of Handy's method to resemble the rotating CT scanner disclosed by Dobbs because any imaging modality that can identify implanted magnetic particles would be suitable in the invention and would constitute mere substitution of well known-equivalents in the art. Furthermore, although the frequency of rotation is not explicitly disclosed by Dobbs, it is highly unlikely that the patient is rotated at a speed greater than 10Hz; in fact the rotating speed would obviously be much lower than 10 rotations per second because rotation speeds that high could induce nausea or injury in the patient.

44. Claim 45 is rejected under 35 U.S.C. 103(a) as being unpatentable over Kraus in view of Cha (US 7073513 B2).

45. Kraus is silent as to the electromagnets of the magnetic field generator being constructed from a high temperature superconductor. However, Cha discloses a method of manipulating implanted magnetic particles using high temperature superconducting coils (col. 1, lines 56-58). It would have been obvious to one of ordinary skill in the art at the time of the invention to construct the electromagnets taught by Kraus from a high temperature superconductor because Cha teaches that conventional materials and methods have drawbacks in that they produce a large amount of heat (col. 1, lines 48-51); this drawback can be overcome by using high temperature superconductors.

Conclusion

46. The prior art made of record and not relied upon is considered pertinent to applicant's disclosure. Method of using magnetic particles to disrupt undesirable tissue under the influence of an external alternating magnetic field: Jin (US 2007/0196281 A1) and Gleich (US 7300452 B2).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to CATHERINE E. BURK whose telephone number is (571) 270-7130. The examiner can normally be reached on Monday-Thursday 9:00 am - 7:00 pm Eastern Time.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Charles Marmor II can be reached on (571) 272-4730. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/C. E. B./
Examiner, Art Unit 3735

/Charles A. Marmor, II/
Supervisory Patent Examiner
Art Unit 3735